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August 24, 2004

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Art Unit: 1637
Examiner: T.E. Strzelecka
Conf. No.: 8452

Re: U.S. Patent Appln. Serial No. 09/404,520 filed September 23, 1999
Inventors: Yongwei CAO *et al.*
Title: Emericella Nidulans Genome Sequence on Computer Readable Medium and Uses Thereof
Atty Dkt.: 16517.081

Sir:

Transmitted herewith for appropriate action by the U.S. Patent and Trademark Office (PTO) are the following documents:

1. Appellants' Brief (in triplicate), with attached Appendix A; and
2. Return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier.

Authorization is hereby given to charge the statutory fee of $330.00 for filing Appellants' Brief to Arnold & Porter LLP Deposit Account No. 50-2387, referencing docket number 16517.081. A duplicate copy of this letter is enclosed.

In the event that extensions of time beyond those petitioned for herewith are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. Appellants do not believe any additional fees are due in conjunction with this filing. However, if any fees are required in the present application, including any fees for extensions of time, then the Commissioner is hereby authorized to charge such fees to Arnold & Porter LLP Deposit Account No. 50-2387, referencing docket number 16517.081. A duplicate copy of this letter is enclosed.

Sincerely,

Thomas E. Holsten (Reg. No. 46,098)
David R. Marsh (Reg. No. 41,408)

Enclosures

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re Patent Application of:	Confirmation No.: 8452
Yongwei CAO *et al.*	Art Unit: 1637
Appln. No.: 09/404,520	Examiner: T.E. Strzelecka
Filed: September 23, 1999	Atty. Docket: 16517.081

For: **Emericella Nidulans Genome Sequence on Computer Readable Medium and Uses Thereof**

APPELLANT'S BRIEF

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

This is an Appeal from the Final Rejection of all claims pending in the above-captioned patent application. A Notice of Appeal was filed on June 24, 2004. Authorization to charge the official fees for this filing is given in the accompanying transmittal letter. *This Brief is submitted in triplicate.*

1. Real Party in Interest

The real party in interest is Monsanto Company, a Delaware corporation with offices at 800 North Lindbergh Boulevard, St. Louis, Missouri 63167.

2. Related Appeals and Interferences

Appellant is unaware of any Appeals or Interferences related to this Appeal.

3. Status of Claims

Claims 58-72 are pending. Claims 1-57 have been cancelled without prejudice to or disclaimer of the subject matter claimed therein. Claims 58-72 stand finally rejected

under 35 U.S.C. §§ 101, 112, first paragraph and 35 U.S.C. § 103. Appellant appeals all of the rejections of claims 58-72.

4. Status of Amendments

Appellant filed a Response to the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures on June 24, 2004. Appellant has not filed any other responses subsequent to Final Rejection in this case.

5. Summary of Invention

The invention is directed to a method of identifying a nucleotide sequence comprising comparing a target sequence to a sequence stored in computer readable medium having recorded thereon at least 100 nucleotide sequences including sequence selected from the group consisting of SEQ ID NO: 16207 through 27905 and complements thereof, and identifying the target sequence as being present in the computer readable medium. Specification at page 34, lines 3-20 and pages 37, line 1 through page 39, line 20. The invention is also directed to methods for identifying a nucleic acid sequence comprising providing a target nucleotide sequence, comparing the target nucleotide sequence to one or more nucleotide sequences stored in a computer readable medium having recorded thereon at least 100 nucleotide sequences including sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof, and identifying the target nucleotide sequence as having significant sequence identity to the one or more nucleotide sequences stored in a computer readable medium.. *Id.* The invention is also directed to a method of detecting a nucleotide sequence comprising, providing a target nucleotide sequence, comparing the target nucleotide sequence to a nucleotide sequence stored in a computer readable medium having recorded thereon at least 100 nucleotide sequences including sequences

selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof, and identifying the target sequence as homologous to the nucleotide sequence. *Id.* The invention is also directed to a method of ranking a target nucleotide sequence by homology to a nucleotide sequence of *E. nidulans* comprising, providing a target nucleotide sequence, comparing the target nucleotide sequence to a nucleotide sequence stored in a computer readable medium having recorded thereon at least 100 nucleotide sequences including sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof, and ranking the target sequence by degree of homology to the nucleotide sequence of *E. nidulans*. *Id.*

6. Issues

The issues in this Appeal are:

(a) whether claims 58-72 are unpatentable under 35 U.S.C. § 101 for allegedly being unsupported by a specific asserted utility or a well established utility;

(b) whether claims 58-72 are unpatentable under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement because the claimed invention purportedly lacks utility;

(c) whether claims 58-72 are unpatentable under 35 U.S.C. § 101 for allegedly containing non-patentable subject matter; and

(d) whether claims 58-72 are unpatentable under 35 U.S.C. §103(a), as allegedly being obvious over Rodriguez-Tome *et al.*

7. Grouping of Claims

Claims 58-72 remain in this case. Claims 58, 59, 67 and 71 are independent. All of the claims at issue do not stand or fall together. A copy of the claims on appeal is attached hereto as Appendix A.

8. Argument

A. Summary of Appellant's Position

As the Supreme Court said in *Brenner v. Manson*, the "basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility...where specific benefit exists in currently available form." 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 695 (1966). Appellant has met their part of the bargain – they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example use to identify the presence or absence of a polymorphism in a population of soybean plants. This benefit is specific, not vague or unknown, and it is a "real world" or substantial benefit. Because the claimed nucleic acid molecules provide at least these benefits, they satisfy the utility requirement of 35 U.S.C. § 101. Because the specification teaches how to make and use the claimed nucleic acid molecules for the disclosed utilities, the enablement requirement of 35 U.S.C. § 112 has been met.

Furthermore, the claims, as a whole, are directed to methods of identifying, detecting and ranking nucleic acid sequences, and as such are directed to a practical application. Such practical applications are at the heart of the statutory subject matter inquiry. Moreover, the claimed methods are not taught or suggested in the cited references. As such, the claims are not obvious.

B. The Claimed Invention Has Legal Utility

Claims 58-72 stand rejected under 35 U.S.C. § 101 as the claimed invention allegedly lacks patentable utility. Final Action mailed March 24, 2004 ("Final Action"), at page 8.

The Examiner has acknowledged that "[c]laims 58-72 are drawn to methods of identifying a nucleotide sequence comprising comparing target sequence to a sequence stored in a computer readable medium having recorded thereon at least 100 nucleotide

sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof." *Id.* The Examiner goes on to allege that "[p]atentability of these claims is based on a computer readable medium with at least 100 nucleic acid sequences recorded thereon. *Id.* The basis for the Examiner's rejection are that: (1) "there is no indication in the specification of what are the functions of any of the sequences with SEQ ID NO: 16207-27905;" (2) "the disclosed uses are generally applicable to any sequence data recorded on computer readable medium;" and (3) "further characterization of the claimed subject matter would be required to identify or reasonably confirm a 'real world' use."

The Examiner's analysis misstates the nature of the asserted uses, ignores disclosed utilities, and misapplies the doctrine of "practical utility" developed by the courts after *Brenner v. Manson*. The "threshold for utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). Furthermore, an invention need only provide one identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) ("when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown").

Initially, claims must be considered as a whole in determining compliance with § 101. *Diamond v. Diehr*, 450 U.S. 175, 188, 209 U.S.P.Q. 1, 9 (1981). It is inappropriate to dissect claims and consider some elements while ignoring others. *Id.* Appellant respectfully submits that they are not claiming the "computer readable medium with at least 100 nucleic acid sequences recorded thereon" in the abstract. Appellant has disclosed sequences of *E. nidulans* that comprise virtually the entire genome of this organism. The amended claims however are directed as a whole to methods of

identifying, detecting or ranking nucleotide sequences where the methods comprise, *inter alia*, the use of a "computer readable medium with at least 100 nucleic acid sequences recorded thereon." Accordingly, the Examiner's assertion that the patentability of the claims is based on the computer readable medium alone is improper.

Furthermore, the courts have expressed a test for utility that hinges on whether an invention provides an "identifiable benefit." *Juicy Whip*, 185 F.3d at 1366, 51 USPQ.2d at 1702. For analytical purposes, the requirement for an "identifiable benefit" may be broken into two prongs: (1) the invention must have a specific, *i.e.*, not vague or unknown benefit, *In re Brana*, 51 F.3d 1560, 1565, 34 U.S.P.Q.2d 1436, 1440 (Fed. Cir. 1995); and (2) the invention must provide a real world, *i.e.*, practical or "substantial" benefit. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). A corollary to this test for utility is that the invention must not be "totally incapable of achieving a useful result," *i.e.*, the utility must not be incredible or unbelievable. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992).

Appellant has asserted in the specification that the claimed methods provide identifiable benefits, for example for transcription profiling, identifying counterpart genes in other species and identifying open reading frames (ORFs). *See, e.g.*, specification page 2, lines 10 through 13 and page 38, lines 11 through 14. Another disclosed use of the claimed methods is in the detection of the presence, absence or level of an organism, for example *E.* nidulans, in a given sample. See, *e.g.* page 37, lines 7 through 9 and page 30, lines 19 through 21. Any one of the above uses is enough to satisfy the § 101 requirement. Because Appellant need only establish a single utility to satisfy 35 U.S.C. § 101, and have done so in the present case, the premise of the rejection under Section 101 is incorrect, and the rejection should be reversed.

(1) The Claimed Methods Provide A Specific Benefit, *i.e.*, They Have Specific Utility

The Examiner ignores the disclosed utilities of the claimed methods and simply argues that the nucleic acid molecules used in the methods lack patentable utility. More specifically, the Examiner alleges that the patentability of the "claims is based on a computer readable medium with at least 100 nucleic acid sequences recorded thereon." Final Action at page 8.

The specification describes multiple utilities for the present invention, including for transcription profiling, identifying counterpart genes in other species and identifying open reading frames (ORFs). *See* specification at page 2, line 10-13 and page 38, lines 11-14. Moreover, the specification also discloses additional utilities for the claimed methods, including use of the methods to rank nucleic acid sequences based on degree of homology to a target sequence. *See*, specification at page 40, lines 10-19.

The Examiner ignores these utilities and argues that "patentability of these claims is based on a computer readable medium with at least 100 nucleic acid sequences recorded thereon" and concludes that such uses are not "considered to be specific and substantial in view of the limited information provided in the specification." *Id.* Even assuming *arguendo* that the Examiner's assertion that the patentability of the claims is based on the computer readable medium, the utility requirement is still met by the disclosure of the specific utilities for the nucleic acid sequences in the specification.

(a) Detecting the Presence or Absence of an Organism

More particularly, one of the utilities disclosed in the specification is use of the nucleic acid sequences of the claimed methods to detect the presence, absence or level of an organism, for example *E. nidulans*, in a given sample. Specification at page 37, lines 7-9 and page 30, lines 19-21. The Examiner argues that this utility, like many of the asserted utilities, is not specific or substantial, but does not provide any support (legal or

factual) for the proposition that detection of organisms in a sample using the claimed nucleic acid methods is not a legal utility. *See, e.g.,* Final Action at page 8.

Many of the disclosed utilities in this case, including the detection of organisms in a sample, are directly analogous to the utilities of a microscope, *i.e.*, the nucleic acid molecules may be used to locate and measure nucleic acid molecules within a sample, cell, or organism. The Examiner denigrates such utilities by asserting that these utilities are not "useful" because they are non-specific uses. Final Action at pages 7-9. However, the fact that, *e.g.*, a new and nonobvious microscope or screening assay can be used for learning about products or processes does not lessen the fact that such "tools" have legal utility. "Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have clear, specific and unquestionable utility (*e.g.*, they are useful in analyzing compounds)." MPEP § 2107.01 at page 2100-33.

Use of the claimed nucleic acid methods to detect the presence, absence or level of an organism in a sample is no more legally insufficient than using a gas chromatograph to analyze the chemical composition of a gas – such use determines information about the gas, not the gas chromatograph. Even if the gas chromatograph detects the absence of a particular chemical element in the gas, that finding does not obviate the utility of the gas chromatograph itself. Information has been obtained about the gas.[1] Likewise, the claimed methods have utility even if the absence of a particular organism is detected. Indeed, the absence of an organism usefully demonstrates that the sample being tested is free of contamination.

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[1] For example, gas sampled from crude oil may be analyzed by gas chromatography for the presence or absence of chlorine, which is toxic to catalysts used in gasoline refining even in very low concentrations. The absence of a peak at the molecular weight of chlorine indicates the absence of chlorine in the sample being tested, thereby providing useful information (no chlorine is present, therefore the catalyst will not be destroyed) to the refinery manager. *See, e.g.*, U.S. Patent No. 6,133,740 entitled "Chlorine Specific Gas Chromatographic Detector."

The nucleic acid sequences of the claimed methods have been asserted to work for a specific, *i.e.*, not vague or unknown benefit, to identify the presence, absence or level of an organism in a sample. This benefit is immediately realized directly from the use of the claimed methods, not from the use of other methods. Such a proven use that provides an acknowledged known benefit to the public satisfies the utility requirement of 35 U.S.C. § 101.

(b) Identifying Counterpart Genes and Regulatory Elements

Other uses for the nucleic acid sequences of the claimed methods are identifying counterpart genes in other species. The specification discloses that the nucleic acid molecules used in the claimed methods can be used to isolate counterpart genes in other organisms such as microbial and plant species.[2] Specification at page 2, lines 10-16. The Examiner has not provided any evidence that would reasonably suggest that this cannot be done, and thus has not met the burden of proof required to establish a utility rejection. *See In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). *Accord In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. 288, 297 (C.C.P.A. 1974).

One illustrative example of a molecule that can be isolated using a claimed nucleic acid molecule is the promoter of the gene corresponding to that nucleic acid molecule. Appellant has specifically disclosed that one use of the nucleic acid molecules is to obtain nucleic acid sequences that encode protein homologs or genetic elements such as promoters and transcriptional regulatory elements. Specification at page 28, lines 5-15. The Examiner suggests that such a utility is not specific. Final Action at pages 3

[2] Furthermore, one skilled in the art of hybridization and amplification understands how to design and utilize probes and primers to target a sequence of interest, and therefore it is not necessary for Appellant to provide a laundry list of each and every nucleic acid molecule that can be identified using the claimed nucleic acid molecules. It is not necessary to disclose what is known. *See, Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000).

and 7-9. This is not correct. The claimed nucleic acid molecules, isolated from *Emericella nidulans*, are particularly useful, for example, to identify regulatory elements. *See, e.g.*, specification at page 16, line 13 through page 18, line 2.

In short, the Examiner suggests that the asserted utilities are legally insufficient simply because other molecules can be used for the same purpose, *i.e.*, chromosome walks. That position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) ("An invention need not be the best or the only way to accomplish a certain result..."). Such an argument would imply that a new golf club has no legal utility because other golf clubs can be used for the same purpose, *i.e.*, hitting golf balls. That position must be rejected as it requires reading "into the patent laws limitations and conditions which the legislature has not expressed," a practice condemned by the Supreme Court. *See Diamond v. Chakrabarty*, 447 U.S. 303, 308, 206 U.S.P.Q. 193, 196 (1980), *quoting United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199, 17 U.S.P.Q. 154, 162 (1933).

Moreover, it is factually incorrect that this use is not "specific" to the claimed nucleic acid molecules. The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter active in soybean plants. *See, e.g.*, specification at page 28, lines 5-15 Examples beginning at page 41, line 1, *et. seq.* A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter. Furthermore, even if a random nucleic acid molecule provided a <u>better</u> starting point than the claimed nucleic acid molecules, it would not obviate the utility of the claimed nucleic acid molecules. An invention may be "less effective than existing devices but nevertheless meet the statutory criteria for patentability." *Custom Accessories, Inc. v. Jeffrey-Allan Indus.*, 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).

The Examiner has failed to provide evidence, or even to suggest a reason for believing that the nucleic acid molecules used in the claimed methods could not be so used. Accordingly, the assertion of this utility as a probe for other molecules satisfies the requirements of 35 U.S.C. § 101. *See In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995).

(c) Disclosed Gene Functions

Other utilities disclosed in the specification is use of the claimed nucleic acid molecules to encode the polypeptides identified in Table 2 or fragment thereof. Specification at page 43, line 7 through page 50, line 21 (Example 2) and Table 2. The Examiner argues however, that "there is no indication in the specification of what are the functions of any of the sequences with SEQ ID NO: 16207-27905." Final Action at page 8. More specifically, the Examiner argues that "these functions are putative, i.e., determined on the basis of sequence comparison with a database of sequences." *Id.* at pages 3-4. The Examiner further questions how "comparing a sequence of a chitinase presented by Applicants with a database of sequences differ[s] from comparing a sequence of a chitinase from any other organism with a database of sequences?" *Id.* at page 4. The Examiner concludes that "there is nothing unique about this process, therefore it does not confer either specific or substantial utility on Applicants' sequences." *Id.* While the Examiner generally questions whether the sequences encode the genes identified in Table 2, the Examiner provides no support to show that any of the SEQ ID NOs do not function as described by the specification.

The specification provides evidence based on sequence identity that the nucleic acid molecules encode polypeptides having identity to various known genes. *See, e.g.*, Table 2. The specification also a detailed description of the identification of the enzymes listed in Table 2. *See, e.g.*, specification at page 43, line 7 through page 50, line 21 (Example 2). The Examiner has provided no evidence to rebut these utilities.

An examiner must accept a utility by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992). "More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such as assertion." Federal Register 66(4):1096, Utility Guidelines (2001). "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 U.S.P.Q.2d 1895, 1900 (Fed. Cir. 1996).

The nucleic acid molecules have been asserted to encode polypeptides having significant identity to various proteins, for example, SEQ ID NO: 16218 encodes a polypeptide having identity to a chitinase. The specification provides ample correlation between the nucleic acid molecules and the specified proteins. Accordingly, the assertion of the use of the nucleic acid molecules to encode, for example a chitinase, or fragment thereof satisfies the utility requirement of 35 U.S.C. § 101.

Moreover, the Examiner's assertion that because "there is nothing unique about this process, ... it does not confer either specific or substantial utility" is wrong as a matter of law. As argued above, there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stifung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) ("An invention need not be the best or the only way to accomplish a certain result..."). The Examiner has provided no evidence that the nucleic acid molecules of the claimed methods cannot be used for the asserted utilities.

(2) The Nucleic Acid Molecules Used in the Claimed Methods Provide Practical, Real World Benefits, *i.e.*, They Have Substantial Utility

The Final Action also suggests that the disclosed uses are legally insufficient because they are not "substantial" utilities. Final Action at pages 6-9. The touchstone of "substantial" utility is "real world" or "practical utility." *See, e.g., Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). " 'Practical utility' is a shorthand way of attributing 'real world' value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." *Nelson v. Bowler*, 626 F.2d 853, 856, 857, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980) ("tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use").[3]

There can be no question that one skilled in the art can use the nucleic acid molecules used in the claimed methods in a manner which provides an immediate benefit to the public, for example to detect the presence, absence or level of an organism in a sample. The detection of organisms provides an immediate benefit to the public because, *e.g.*, it enables a person to identify contaminated samples. This information about a sample's profile, like the information about a compound's pharmacological profile in *Nelson*, provides an immediate benefit and thus a practical utility to the public.

Quite apart from the detection of organisms in a sample, there is also no question that the public has recognized the benefits provided by the claimed subject matter, and has attributed "real world" value to such nucleic acid molecules. The utility of genomic sequences is not merely an academic issue; the real world value of genomic sequences is self-evident from the growth of a multi-million dollar industry in the United States

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[3] *Accord Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747-48 (Fed. Cir. 1985); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. 453, 454 (C.C.P.A. 1974).

premised on the usefulness of genomic sequences. Like fermentation processes involving bacteria, genomic sequences are "industrial product[s] used in an industrial process – a useful or technical art if there ever was one." *In re Bergy*, 563 F.2d 1031, 1038, 195 U.S.P.Q. 344, 350 (C.C.P.A. 1977).

The market participants for genomic products are primarily sophisticated corporations and highly knowledgeable scientists who are unlikely to pay for useless inventions. *Cf. Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960, 220 U.S.P.Q. 592, 599 (Fed. Cir. 1983) ("People rarely, if ever, appropriate useless inventions"). Quite simply, the commercial value of genomic sequences is proof of their real world value and of the benefits they provide to the public. This evidence cannot be ignored. The patent system was created to serve and foster growth and development in the industrial arts. If the industries themselves recognize and appreciate the value of an invention, it is not for the Patent Office to say that they are mistaken.

(3) The Disclosed Utilities Are Credible to One of Skill in the Art

An assertion of utility must be accepted by the Examiner unless it would not be considered "credible" by a person of ordinary skill in the art. MPEP § 2107 at 2100-29. Cases in which utility was found not to be credible are rare, and usually involve "hare-brained" utilities.[4] A challenge to the credibility of a utility is essentially a challenge

[4] Examples of incredible utilities are given in MPEP § 2107.01 at page 2100-34, and include:

> an invention asserted to change the taste of food using a magnetic field (*Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 U.S.P.Q. 848 (Fed. Cir. 1985)), a perpetual motion machine (*Newman v. Quigg*, 877 F.2d 1575, 11 U.S.P.Q. 1340 (Fed. Cir. 1989)), a flying machine operating on "flapping or flutter function" (*In re Houghton*, 433 F.2d 820, 167 U.S.P.Q. 687 (C.C.P.A. 1970)), a method for increasing the energy output of fossil fuels upon combustion through exposure to a magnetic field (*In re Ruskin*, 354 F.2d 395, 148 U.S.P.Q. 221 (C.C.P.A. 1966)), uncharacterized compositions for curing a wide array of cancers (*In re Citron*, 325 F.2d 248, 139 U.S.P.Q. 516 (C.C.P.A. 1963)), a method of controlling the aging process (*In re Eltgroth*, 419 F.2d 918, 164 U.S.P.Q. 221 (C.C.P.A. 1970)), and a method of restoring hair growth (*In re Ferens*, 417 F.2d 1072, 163 U.S.P.Q. 609 (C.C.P.A. 1969)).

directed to operability, and such a challenge must be supported by a clear statement of "factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); MPEP § 2107.02 at 2100-41.

Appellant has explicitly identified specific and substantial utilities in the specification. "To violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992). To date, the Examiner has provided no evidence that the claimed methods will not work for the disclosed utilities. Unless and until the Examiner can prove that the claimed invention is wholly inoperative, the rejection must be withdrawn.

In view of the above, Appellant contends that the claimed methods are supported by credible, specific, and substantial utilities disclosed in the specification. Moreover, the Examiner has failed to raise any credible evidence challenging the presently asserted utilities. Consequently, the rejection of claims 58-72 under 35 U.S.C. §101 is improper and should be reversed.

C. The Claimed Methods Are Enabled by the Specification

The enablement of the claimed methods has been challenged. Claims 58-72 stand rejected as not enabled by the specification, because the nucleic acid molecules used in the claimed methods allegedly lack utility and therefore cannot be enabled. Final Action at page 9. This rejection is erroneous and has been overcome by the arguments stated above regarding utility because it is well-established law that "the enablement requirement is met if the description enables <u>any</u> mode of making and using the invention." *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*,

946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). Unless and until the Examiner comes forth with evidence to rebut the objective truth of the utilities disclosed in the specification, this enablement rejection must be withdrawn as improper. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement).

D. The Claimed Methods Define a Statutory Subject Matter Under 35 U.S.C. § 101

Claims 58-72 stand rejected apparently because the claims encompass non-functional descriptive material and therefore do not qualify as patentable subject matter. Final Action at page 10.

In particular, the Examiner quotes MPEP section 2106.IV.B.1(b) and highlights several passages within this section relating to "nonfunctional descriptive material." Final Action at pages 9-10. The Examiner argues that "[s]equences stored on a computer readable medium are therefore considered as non-functional descriptive material." *Id.* at page 10. The Examiner also argues that "[c]omparing a sequence (a non-functional descriptive material) to another sequence (a non-functional descriptive material) results in a string of data, which also constitute non-functional descriptive material, since no physical transformation of the data has occurred outside of the computer." *Id.* at page 7. This ground of rejection is improper.

The Supreme Court has interpreted 35 U.S.C. § 101 broadly,[5] finding "that Congress intended statutory subject matter to 'include anything under the sun that is made by man.'" *AT&T Corp. v. Excel Commun., Inc.*, 172 F.3d 1352, 1355, 50

[5] 35 U.S.C. § 101 provides: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."

U.S.P.Q.2d 1447 (Fed. Cir. 1999) (quoting *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980). The bounds of § 101 are not limitless however, as the Court has specifically identified three categories of unpatentable subject matter: "laws of nature, natural phenomena and abstract ideas." *See, e.g., Diamond v. Diehr*, 450 U.S. 175, 185, 209 U.S.P.Q. 1, (1981).

Claims must be considered as a whole in determining compliance with § 101. *Diamond v. Diehr*, 450 U.S. 175, 188, 209 U.S.P.Q. 1, 9 (1981). It is inappropriate to dissect claims and consider some elements while ignoring others. *Id.* The appealed claims are directed as a whole to methods of identifying, detecting or ranking nucleotide sequences where the methods comprise, *inter alia*, the use of a "computer readable medium with at least 100 nucleic acid sequences recorded thereon." Accordingly, the Examiner's assertion that the patentability of the claims is based on the computer readable medium alone is improper.

"A series of steps is a 'process' within § 101 unless it falls within a judicially determined category of nonstatutory subject matter exceptions." *In re Sarkar*, 588 F.2d 1330, 1333, 200 USPQ 132, 137 (CCPA 1978). As mentioned above, the courts have recognized several narrow exceptions for "laws of nature, natural phenomena, and abstract ideas." *See, e.g., In re Alappat*, 33 F.3d 1526, 1542, 31 USPQ.2d 1545, 1556 (Fed. Cir. 1994) (in banc) (citing *Diamond v. Diehr*, 450 U.S. 175, 185 (1981)). The heart of the statutory subject matter inquiry is whether the claimed subject matter as a whole is directed to a "practical application," which the courts have defined as "a useful, concrete and tangible result. *State Street Bank & Trust Co. v. Signature Financial Group, Inc.*, 149 F.3d 1368, 1375, 47 USPQ.2d 1596, 1602 (Fed. Cir. 1998).

The appealed claims are directed to methods of identifying, detecting or ranking a nucleotide sequence comprising comparing a target sequence to a sequence stored in computer readable medium having recorded thereon at least 100 nucleotide sequences

including sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof. Accordingly, the claims define a process. The Examiner has not provided any evidence that the claimed methods fall into one of the narrow exceptions. Moreover, the claimed methods are directed to a "practical application."

(1) The Claimed Methods Are Directed to a Practical Application

The Examiner appears to require the claimed methods to "result in concrete and tangible products resulting in a physical transformation outside the computer." Final Action at page 7. The courts have noted that "[t]he notion of 'physical transformation' can be misunderstood." *AT&T Corp. v. Excel Commun., Inc.*, 172 F.3d 1352, 1358, 50 U.S.P.Q.2d 1447, 1453 (Fed. Cir. 1999). The Federal Circuit noted that a physical transformation "is not an invariable requirement, but merely one example of how a mathematical algorithm may bring about a useful application." *Id.*

The Examiner's requirement that a physical transformation occur "outside the computer" is wrong as a matter of law. First, as noted above, the Federal Circuit has stated that a "physical transformation" is not the only means to bring about a useful application. 172 F.3d at 1358, 50 U.S.P.Q.2d at 1453. The transformation of data from one form to another has been found to satisfy § 101 where the produced data had specific meaning. *See, e.g., AT&T Corp*, 172 F.3d 1352, 50 U.S.P.Q.2d 1447, *Arrhythmia Research Technology, Inc. v. Corazonix Corp.*, 958 F.2d 1053, 22 U.S.P.Q.2d 1033 (Fed. Cir. 1992). The data produced by the claimed methods have specific meaning, for example as having substantial identity to the nucleic acid sequences on the computer readable medium.

Moreover, the Examiner's requirement for a "physical transformation" is against Patent Office procedure. The MPEP provides that for a process claim involving a computer-related step to be statutory, the process must either: "(A) result in a physical

transformation outside the computer for which practical application in the technological arts is either disclosed in the specification or would have been known to a skilled artisan, or (B) be limited to a practical application within the technological arts." MPEP 2106 B.2.(b) at page 2100-15. "A method is limited to a practical application when the method, as claimed, produces a concrete, tangible and useful result. *Id.* at page 2100-18 (citing *AT&T Corp.*, 172 F.3d at 1358, 50 U.S.P.Q.2d at 1452).

The claimed methods are directed to "practical applications." The claims are directed to methods of identifying, detecting and ranking nucleic acid sequence through the steps of comparing a target sequence to a sequence stored in computer readable medium having recorded thereon at least 100 nucleotide sequence including sequence selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof. These methods produce useful, concrete and tangible results of identifying, detecting or ranking nucleotide sequences within the biotechnological arts.

Furthermore, assuming *arguendo* that the sequences stored on a computer readable medium are non-functional descriptive material and are therefore not patentable subject matter alone, this fact would not render the instantly claimed methods unpatentable. Such a situation is analogous to the use of mathematical algorithms in claimed methods. A mathematical algorithm in the abstract may not qualify as patentable subject matter, yet the Federal Circuit has found methods reciting steps involving mathematical algorithms to fit within the statutory subject matter. *See, e.g., AT&T Corp. v. Excel Commun., Inc.*, 172 F.3d 1352, 50 U.S.P.Q.2d 1447 (Fed. Cir. 1999). The claimed methods recite a step involving comparing a target sequence to a sequence stored in computer readable medium having recorded thereon at least 100 nucleotide sequences including the sequences of SEQ ID NO: 16207 through SEQ ID NO: 27905. As argued above, this step is used in a method that provides the "useful, concrete and tangible result" -- identifying a nucleotide sequence.

Accordingly, the claimed methods are patentable subject matter. Consequently, the rejection of claims 58-72 as non-functional descriptive material is improper.

E. The Claimed Methods are Not Obvious

Claims 58-72 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Rodriguez-Tome *et al.* (Nucl. Acids Res., vol. 24, pp. 6-12, 1996). Final Action at pages 10-11. This rejection is respectfully traversed for at least the reasons which follow.

The Examiner argues that "Rodriguez-Tome et al. teach CD-ROM with containing EMBL nucleotide sequence database." *Id.* at page 10.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. The teaching or suggestion to make the claimed combination must be found in the prior art, and not be based on Applicant's disclosure. *See* M.P.E.P. §§2143.01 and 2143.03.

In a proper obviousness determination, the changes from the prior art must be evaluated in terms of the whole invention, including whether the prior art provides any teaching or suggestion to one of ordinary skill in the art to make the changes that would produce the claimed invention. *See In re Chu,* 36 U.S.P.Q.2d 1089, 1094 (Fed. Cir. 1995). This includes what could be characterized as simple changes. *See, e.g., In re Gordon,* 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984) (Although a prior art device could have been turned upside down, that did not make the modification obvious unless the prior art fairly suggested the desirability of turning the device upside down.).

Only when the prior art teaches or suggests the claimed invention does the burden fall on the applicant to rebut that *prima facie* case. *See In re Dillon,* 16 U.S.P.Q.2d 1897,

1901 (Fed. Cir. 1990) (in banc), *cert. denied,* 500 U.S. 904 (1991). However, a *prima facie* case of obviousness may be rebutted by showing that the art, in any material respect, teaches away from the claimed invention.

The present invention is drawn to methods of identifying, detecting and ranking nucleic acid sequences comprising, *inter alia*, comparing target nucleotide sequences to one or more nucleotide sequences stored in a computer readable medium having recorded thereon at least 100 nucleotide sequences including sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof.

(1) Rodriguez-Tome does not teach or suggest all of the elements

The Examiner asserts that Rodriguez-Tome *et al.* teach a CD-ROM having EMBL nucleotide sequences, as well as software for data query. Final Action at pages 10-11. The Examiner further alleges that Rodriguez-Tome *et al.* further teaches "comparing users' sequences (=target sequences) to sequence in the EMBL nucleotide sequence database." *Id.* at page 11. However, whatever else Rodriguez-Tome *et al.* discloses or suggests, it does not disclose or suggest a computer readable medium having recorded thereon at least 100 nucleotide sequences including sequence selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof.

The Examiner has alleged that it "would have been *prima facie* obvious to one of ordinary skill in the art to have used a computer system comprising a CD-ROM of Rodriguez-Tome et al. to perform sequence searches against a collection of sequence data. Final Action at page 11. The Examiner asserts that the ordinary practitioner would have been motivated because using CD-ROM databases would make database searches "accessible to clients without Internet Access." *Id.*

The mere fact that references can be modified does not render the resultant modification obvious unless the prior art also suggests the desirability of the modification. M.P.E.P. § 2143.01; *In re Mills,* 16 U.S.P.Q.2d 1430, 1432 (Fed. Cir.

1990); *see also, In re Fritch,* 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992). This includes what could be characterized as simple changes. *See Gordon*, 221 U.S.P.Q. at 1127. Even changes that are allegedly "merely a matter of engineering design choice" require a suggestion of desirability in the prior art. *See In re Kuhle*, 188 U.S.P.Q. 7, 9 (CCPA 1975). In *Kuhle*, the element in question as the "obvious matter of design choice" was obvious because it was "notoriously old with the common flashlight." *Id.* at 8. As such, the prior art did contain a teaching that suggested the modification in question to one of ordinary skill in the art, thereby establishing a *prima facie* case of obviousness.

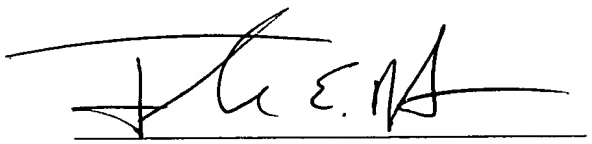
In the present case, the deficiencies in the teachings of Rodriguez-Tome *et al.* regarding the nucleotide sequence stored in a computer readable medium having recorded thereon at least 100 nucleotide sequences including sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof are not compensated for by any other reference. As such, Rodriguez-Tome *et al.* does not provide specific motivation to one of ordinary skill in the art such that the skilled artisan would arrive at the present invention upon reading Rodriguez-Tome *et al.*

In sum, the Examiner's conclusion of obviousness is based on improper hindsight reasoning. No suggestion to modify the cited reference has been found in the cited reference or pointed out to Appellant from the general knowledge of one of ordinary skill in the art. For at least these reasons, the Appellant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness, as required by 35 U.S.C. § 103. As such, the rejection of claims 58-72 is improper and should be reversed.

CONCLUSION

In view of the foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the Rejections and that the subject application be allowed forthwith.

Respectfully submitted,



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Filed: August 24, 2004

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APPENDIX A

58. A method of identifying a nucleotide sequence comprising comparing a target sequence to a sequence stored in computer readable medium having recorded thereon at least 100 nucleotide sequences including sequence selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof, and identifying said target sequence as being present in the computer readable medium.

59. A method for identifying a nucleic acid sequence comprising:

a) providing a target nucleotide sequence;

b) comparing said target nucleotide sequence to one or more nucleotide sequences stored in a computer readable medium having recorded thereon at least 100 nucleotide sequences including sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof; and

c) identifying said target nucleotide sequence as having significant sequence identity to said one or more nucleotide sequences stored in a computer readable medium.

60. The method according to claim 59, wherein said target sequence shares between 100% and 90% sequence identity with one or more of said nucleotide sequences stored on a computer readable medium.

61. The method according to claim 60, wherein said target sequence shares between 100% and 95% sequence identity with one or more of said nucleotide sequences stored on a computer readable medium.

62. The method according to claim 61 wherein said target sequence shares between 100% and 98% sequence identity with one or more of said nucleotide sequences stored on a computer readable medium.

63. The method according to claim 62 wherein said target sequence shares between 100% and 99% sequence identity with one or more of said nucleotide sequences stored on a computer readable medium.

64. The method according to claim 59, wherein said target sequence is identified as homologous to an open reading frame (ORF) within said nucleotide sequence stored on a computer readable medium.

65. The method of claim 59, wherein said target sequence is a nucleotide sequence of between about 30 and about 300 nucleotide residues in length.

66. The method of claim 59, wherein said target sequence is identified as homologous to a sequence encoding an *Emericella nidulans* protein or fragment thereof within said one or m ore nucleotide sequences stored on a computer readable medium.

67. A method of detecting a nucleotide sequence comprising:

a) providing a target nucleotide sequence;

b) comparing said target nucleotide sequence to a nucleotide sequence stored in a computer readable medium having recorded thereon at least 100 nucleotide sequences

including sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof; and

c) identifying said target sequence as homologous to said nucleotide sequence.

68. (New) The method according to claim 67, wherein said target sequence is homologous to an open reading frame (ORF) within said nucleotide sequence.

69. The method of claim 67, wherein said target sequence is a nucleotide sequence of between about 30 and about 300 nucleotide residues in length.

70. The method of claim 67, wherein said target sequence is identified according to degree of homology to said nucleotide sequence stored in a computer readable medium.

71. A method of ranking a target nucleotide sequence by homology to a nucleotide sequence of *E. nidulans* comprising:

a) providing a target nucleotide sequence;

b) comparing said target nucleotide sequence to a nucleotide sequence stored in a computer readable medium having recorded thereon at least 100 nucleotide sequences including sequences selected from the group consisting of SEQ ID NO: 16207 through SEQ ID NO: 27905 and complements thereof; and

c) ranking said target sequence by degree of homology to said nucleotide sequence of *E. nidulans*.

72. The method of claim 71, wherein said target sequence is a nucleotide sequence of between about 30 and about 300 nucleotide residues in length.